FINAL ACTION

1. Applicant's amendments and responses filed January 25, 2008 is acknowledged. Claims 1, 7, 17, 27-36 and 48 have been amended. Claims 10 and 20 have been canceled. Claims 23-26 and 37-44 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-9, 11-19, 21-22, 27-36 and 45-48 are under examination.

Rejections Withdrawn

2. In view of Applicant's amendments the following rejections are withdrawn:

(a) rejection of claim 20 under 35 U.S.C. 112 first paragraph, pages 3-6, paragraph 3.
(b) rejection of claim 2 under 35 U.S.C. 112 second paragraph, page 7, paragraph 5.
c) rejection of claim 48 under 35 U.S.C. 112 second paragraph, page 6, paragraph 4.

Rejections Maintained

3. The rejection under 35 U.S.C. 103(a) is maintained for claims 1-3, and 5-6 for the reasons set forth on pages 7-9 paragraph 6 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The claims are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al *(Journal of Fish Diseases, 2000, 23, 137-145)* in view of Yang et al *(U.S. Patent No. 6,872,386 published March 29, 2005)*.

Claims 1-3, 5-6 and 10 are drawn to an oral vaccine comprising in an orally suitable formulation, at least one of isolated recombinant adhesion protein of *Aeromonas hydrophila* (AHMA) selected from the group consisting of isolated recombinant adhesion proteins having the amino acid sequence as set forth in any one of SEQ Id Nos: 2, 4, or 8, wherein said vaccine is capable, by oral administration in an immunologically sufficient amount of effecting immunization an animal against *Aeromonas hydrophila*.

Fang et al teach a vaccine composition comprising the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* and Freund's complete adjuvant (see the Abstract and page 139). Fang et al teach that the vaccine composition contained 150 $\mu g\ mL^{-1}$ of the protein (page 139). Claim limitations such as "wherein the proportion of water and oil in the emulsion further comprise 1:2, "wherein the proportion of water in the emulsion is equal" are being viewed as limitations of experimental design choice.

Fang et al do not teach "oral administration".

Yang et al teach that oral administration has advantages because it is non-stressful, requires little labor, and can be applied at a large scale. Yang et al discloses oral vaccines that are effective, although oral vaccines taught in the art have not been successful (column 1). Yang et al teach that the oral vaccines of the invention comprise more than one antigen. Yang et al teach oral vaccines that comprise multiple antigens produce immune response from the same or different pathogens (column 2).

It would be prima facie obvious at the time the invention was made to prepare a vaccine that is suitable for oral administration because Yang et al teach that oral administration has advantages because it is non-stressful, requires little labor, and can be applied at a large scale. It would be expected absent evidence to the contrary, that the vaccine as taught by Fang et al would be effective if formulated in an oral suitable form because Yang et al have demonstrated that orally administered vaccines are effective in treating aquatic animals.

Applicant's Arguments

Applicant urges that one of ordinary skill reading Yang et al would not have been led to the current invention. Applicant urges that by this reading, one of skill in the art would expect an oral vaccine comprising an isolated recombinant protein would be ineffective. Applicant refers the Examiner to Example VIII of the instant specification.

Applicant urges that Fang et al teach intraperitoneal immunization and not oral immunization. Applicant urges that if one did combine the intraperitoneally administered protein of Fang et al with the method of Yang et al the result would not be

an oral vaccine comprising an isolated recombinant AHMA protein capable of effecting immunization of a fish against *Aeromonas hydrophila* as claimed. Applicant urges that the Office has failed to establish a case of *prima facie* obviousness.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

In response to applicant's argument that no case of *prima facie* obviousness was established, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Fang et al teach a vaccine composition comprising the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* and Freund's complete adjuvant administered intraperitoneally. Fang et al does not teach oral administration. However, Yang et al teach administering fish vaccines by oral administration. Yang et al teach that oral administration has advantages because it is non-stressful, requires little labor, and can be applied at a large scale. One of ordinary skill in the art, would reasonably conclude that fish vaccines can be administered orally because oral administration is non-stressful, requires little labor, and can be applied at a large scale. In other words, oral

administration has the before stated advantages over intraperitoneal administration of fish vaccines.

Applicant is reminded that it is the combination of prior art references that teach the claimed invention and not one individual reference. Therefore, Fang et al or Yang et al individually need not disclose the claimed invention.

To address Applicant's comments regarding an isolated recombinant protein would be ineffective, it should be noted that the term "recombinant" is a process limitation in the product claim, however, Yang et al teach that recombinant antigens can be used as a part of fish or aquatic vaccines. See the Abstract. There is nothing on the record to show that the combination of prior art reference does not teach or suggest the claimed invention.

In view of all of the above, this rejection is maintained.

4. The rejection under 35 U.S.C. 103(a) is maintained for claim 4 for the reasons set forth on page 9 paragraph 7 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim 4 is rejected under 35 U.S.C. 103(a) unpatentable over Fang et al *(Journal of Fish Diseases, 2000, 23, 137-145)* in view of Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* as applied to claims 1-3, 5-6 and 10 above and further in view of Chen et al *(U.S. Patent No. 6,720, 001 B1, published April 13, 2004).*

Claim 4 is drawn to the oral vaccine of claim 3 further comprising palm oil.

Fang et al and Yang et al as combined above do not teach palm oil.

Chen et al teach that the organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (Abstract, columns 5 and 6). Chen et al teach that the compositions of the invention that contain organic oils such as palm oil are stable compositions (column 5).

It would be *prima facie* obvious at the time the invention was made to add the palm oil as taught by Chen et al to the vaccine composition of Fang et and Yang et al as

combined above because Chen et al teach the that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (columns 5 and 6). It would be expected barring evidence to the contrary that a vaccine comprising palm oil would be effective stabilizing vaccines at improving delivery of polyfunctional active ingredients.

Applicant's Arguments

Applicant urges that Chen et al 's disclosure of palm oil do not overcome the deficiencies of Fang et al in view of Yang et al.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

Chen et al teach the that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (Abstract, columns 5 and 6). It is the Examiner's position that the combination of references (Fang et al, Yang et al and Chen et al) renders the claimed invention obvious.

In view of all of the above this rejection is maintained.

5. The rejection under 35 U.S.C. 103(a) is maintained for claims 7-9 for the reasons set forth on pages 9-10 paragraph 8 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claims 7-9 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al *Journal of Fish Diseases, 2000, 23, 137-145)* in view of Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* as applied to claims 1-3, 5-6 and 10 and further in view of Calanchi et al *(U.S. Patent No. 5,008,117, published April 16, 1991).*

Claims 7-9 are drawn to the oral vaccine of claim 2 further mixed with a binding agent, wherein the binding agent comprises particulate feed material and wherein the binding agent comprises high viscosity carboxymethylcellose.

The teachings of Fang et al and Yang et al have been described previously (paragraph 5 above).

Fang et al and Yang et al as combined above do not teach binding agents such as carboxymethylcellulose.

Calanchi et al teach that binding agents such as carboxymethylcellulose (column 3). Calanchi et al teach that binders are soluble in water and solvents (column 3). Calanchi et al teach that binders are often used to thicken the composition (column 4). Calanchi et al teach using these thickeners or binding agents in pharmaceutical compositions (column 2, examples and claims).

It would be *prima facie* obvious at the time the invention was made to add carboxymethylcellulose as taught by Calanchi et al to the vaccine composition of Wolf-Fang et al and Yang et al as combined above because Calanchi et al teach that binders are often used to thicken the composition and have the property of dispersing and dissolving quickly in water or aqueous vehicles (see the Abstract). It would be expected barring evidence to the contrary that a vaccine comprising binding agents such as carboxymethylcellulose would be effective in making the components of the composition easily to disperse and dissolve quickly in water or aqueous vehicles.

Applicant's Arguments

Applicant urges that Calanchi et al is relied on for the use of thickening agents e.g. carboxymethylcellulose. Applicant urges that the description in Calanchi et al would not have suggested the invention of claim 7. Applicant urges that the present invention teaches that the oral vaccine comprising a binding agent achieves a "particulate consistency". Applicant urges that in contrast Calanchi et al disclose a formulation that may contain carboxymethylcellulose but expolicity avoids precipitation and particle formation. Applicant urges that Calanchi et al describe particle formation as a disadvantage in the prior art. Applicant urges that a particulate-free formulation as suggested by Calanchi et al would not be useful in the claimed invention. Applicant urges that the description in Calanchi et al does not remedy the deficiencies of Fang et al and Yang et al as discussed above.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

Calanchi et al teach that carboxymethylcellulose is a thickening or suspending agent as well as a water soluble binder. It is the Examiner's position that the combination of references (Fang et al, Yang et al and Calanchi et al) renders the claimed invention obvious.

To address Applicant's comment's regarding column 2, lines 12-27 of Calanchi et al, it should be noted that these comments were made regarding past preparations of microcapsules and not the teachings of Calanchi et al.

To address Applicant's comments regarding "particulate consistency", it should be noted that Applicant is arguing limitations that are not in the claims. The claims do not recite "particulate consistency".

In view of all of the above this rejection is maintained.

6. The rejection under 35 U.S.C. 103(a) is maintained for claims 11-12, 15-16, 20, 27-32, 35-36 and 48 for the reasons set forth on pages 11-13 paragraph 9 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claims 11-12, 15-16, 20, 27-32, 35-36 and 48 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145)* in view of Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005) as*

applied to claims 1-3, 5-6 and 10 above and further in view of Wang et al *(Fish Shellfish Immunol, Nov. 2002;13(5):337-50(Abstract only).*

Claims 11-12, 15-16, 20, 27-32, 35-36 and 48 are drawn to the oral vaccine of claim 1 further comprising recombinant protein comprising immobilization antigen repeat I of *Ichthyophythirius multifiliis.*

The teachings of Fang et al and Yang et al have been described previously (paragraph 5 above).

Fang et al and Yang et al as combined above do not teach a vaccine comprising the immobilization antigen repeat I of *Ichthyophythirius multifiliis.*

Wang et al teach a vaccine composition comprising the immobilization antigen repeat I of *Ichthyophythirius* and Freund's incomplete adjuvant (see the Abstract). Wang et al teach that fish immunized with *Ichthyophythirius multifiliis* (the antigen developed high titers of serum immobilized antibodies (see the Abstract). Wang et al teach that this study shows there is a clear role for the immobilization antigen repeat I of *Ichthyophythirius* in protection (see the Abstract). The claim limitation "recombinant" is being viewed as a process limitation.

Regarding the specific dosages or ranges listed in the instant claims, MPEP 2144.05 states, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)."

It would be *prima facie* obvious at the time the invention was made to add the immobilization antigen repeat I of *Ichthyophythirius* as taught by Wang et al to the vaccine composition of Yang et al because Yang et al teach that the oral vaccine of the invention comprise multiple antigens that induce immune response against the same or different antigens. It would be expected barring evidence to the contrary that a

vaccine comprising proteins from *Aeromonas hydrophila* and immobilization antigen repeat I of *Ichthyophythirius* would be effective in protecting against a broad spectrum of fish diseases.

Applicant's Arguments

Applicant urges that the disclosure of Wang et al of the *Ichthyophythirius multifiliis* antigen does not overcome the deficiencies of Fang et al and Yang et al as described above. Applicant urges that Wang et al, like Fang et al is limited to intraperitoneal injection.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

Wang et al teach a vaccine composition comprising the immobilization antigen repeat I of *Ichthyophythirius* and Freund's incomplete adjuvant (see the Abstract). Wang et al teach that fish immunized with *Ichthyophythirius multifiliis* the antigen developed high titers of serum immobilized antibodies (see the Abstract).

To address Applicant's comments regarding intraperitioneal administration, as stated above Yang et al teach that oral administration has advantages because it is non-stressful, requires little labor, and can be applied at a large scale. One of ordinary skill in the art, would reasonably conclude that oral administration of fish vaccines has advantages over intraperitioneal administration because oral administration is non-stressful, requires little labor, and can be applied at a large scale.

In view of all of the above this rejection is maintained.

7. The rejection under 35 U.S.C. 103(a) is maintained for claims 13-16 for the reasons set forth on pages 13-14 paragraph 10 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claims 13-16 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145),* Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* and Wang et al *(Fish Shellfish Immunol., Nov. 2002;13(5):337-50) (Abstract only)* as applied to claims 1-3, 5-6, 10-12, 15-16, 20, 27-32, 35-36 and 48 above and further in view of Chen et al *(U.S. Patent No. 6,720, 001 B1, published April 13, 2004).*

Claims 13-16 are drawn to the vaccine of claim 12 further wherein said emulsifying oil comprises organic oil, wherein said emulsifying oil comprises palm oil, wherein the proportion of water and oil in the emulsion is the ratio 1:2 and wherein the proportion of water and oil in the emulsion is equal.

The teachings of Fang et al, Yang et al and Wang et al have been described previously (paragraph 8 above).

Fang et al, Yang et al and Wang et al as combined above do not teach organic oil or palm oil.

Chen et al teach that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (columns 5 and 6). Chen et al teach that the compositions of the invention that contain organic oils such as palm oil are stable compositions (column 5).

It would be *prima facie* obvious at the time the invention was made to add the palm oil as taught by Chen et al to the vaccine composition of Fang et al, Yang et al and Wang et al as combined above because Chen et al teach the that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (columns 5 and 6). It would be expected barring evidence to the contrary that a vaccine comprising palm oil would be effective stabilizing vaccines at improving delivery of polyfunctional active ingredients.

Applicant's Arguments

Applicant urges that the combination of prior art references does not teach or suggest the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

As stated above, it is the Examiner's position that the combination of references (Fang et al, Yang et al, Wang et al and Chen et al) renders the claimed invention obvious.

In view of all of the above this rejection is maintained.

8. The rejection under 35 U.S.C. 103(a) is maintained for claims 17-19 for the reasons set forth on pages 14-15 paragraph 11 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claims 17-19 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145),* Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* and Wang et al *(Fish Shellfish Immunol., Nov. 2002;13(5):337-50)(Abstract only)* as applied to claims 1-3, 5-6, 10-12, 15-16, 20, 27-32, 35-36 and 48 above and further in view of Calanchi et al *(U.S. Patent No. 5,008,117, published April 16, 1991).*

Claims 17-19 are drawn to the oral vaccine of claim 12 further mixed with a binding agent, wherein the binding agent comprises particulate feed material and wherein the binding agent comprises high viscosity carboxymethylcellose.

The teachings of Fang et al, Yang et al and Wang et al have been described previously (paragraph 8 above).

Fang et al, Yang et al and Wang et al as combined above do not teach a vaccine comprising carboxymethylcellulose.

Calanchi et al teach that binding agents such as carboxymethylcellulose (column 3). Calanchi et al teach that binders are soluble in water and solvents (column 3). Calanchi et al teach that binders are often used to thicken the composition (column 4). Calanchi et al teach using these thickeners or binding agents in pharmaceutical compositions (column 2, examples and claims).

It would be *prima facie* obvious at the time the invention was made to add carboxymethylcellulose as taught by Calanchi et al to the vaccine composition of Wolf-Fang et al, Yang et al and Wang et al as combined above because Calanchi et al teach that binders are often used to thicken the composition and have the property of dispersing and dissolving quickly in water or aqueous vehicles (see the Abstract). It would be expected barring evidence to the contrary that a vaccine comprising binding

agents such as carboxymethylcellulose would be effective at making the components of the composition easily to disperse and dissolve quickly in water or aqueous vehicles.

Applicant's Arguments

Applicant urges that the combination of prior art references does not teach or suggest the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

As stated above, it is the Examiner's position that the combination of references (Fang et al, Yang et al, Wang et al and Calanchi et al) renders the claimed invention obvious.

9. The rejection under 35 U.S.C. 103(a) is maintained for claim 45 for the reasons set forth on pages 15-18 paragraph 12 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim 45 is rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145)*, Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* and Wang et al *(Fish Shellfish Immunol., Nov. 2002;13(5):337-50)*(Abstract only) as applied to claims 1-3, 5-6, 10-12, 15-16, 20, 27-32, 35-36 and 48 above and in further view of Wolf-Watz et al (*U.S. Patent No. 5,284,653 published February 8, 1994).*

Claims 45 is drawn to the oral vaccine of claim 11 further comprising an inactivated virus selected from the group consisting of guppy reovirus and guppy nervous necrosis virus.

The teachings of Fang et al, Yang et al and Wang et al have been described previously (paragraph 8 above).

Fang et al, Yang et al and Wang et al as combined above do not teach guppy reovirus and guppy nervous necrosis virus.

Wolf-Watz et al teach a fish vaccine comprising live avirulent invasive bacteria (see the Title and the Abstract). Wolf-Watz et al teach that viruses such as infectious pancreatic necrosis virus (guppy reovirus) and infectious hematopoietic necrosis virus may apart of the vaccine of the invention (column 6). Wolf-Watz et al teach that the bacteria of the invention contains $1x10^2$-$1x10^8$ bacteria/ml (column 8). Wolf-Watz et al teach that the vaccine of the invention can be added to fish feed (column 8).Wolf-Watz et al teach that the invention contemplates vaccines comprising bacteria the carry multiple determinants from different pathogenic fish and capable of expressing hybrid (fusion) determinants (column 7).

It would be *prima facie* obvious at the time the invention was made to add the guppy reovirus as taught by Wolf-Watz et al to the vaccine composition of Fang et al, Yang et al and Wang et al as combined above because Yang et al teach oral vaccines that comprise multiple antigens produce immune response from the same or different pathogens (column 2) and Wolf-Watz et al teach that the vaccine of the invention may comprise one or more antigens that are pathogenic to fish to produce a vaccine that provides broad spectrum protection against a range of fish pathogens (column 7). It would be expected barring evidence to the contrary that a vaccine comprising proteins from multiple antigens would be effective in protecting against a broad spectrum of fish diseases.

Applicant's Arguments

Applicant urges that the disclosure of Wolf-Watz et al is relied on for the disclosure of guppy reovirus. However, Wolf-Watz et al not overcome the deficiencies of Fang et al and Yang et al as described above.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

Wolf-Watz et al teach that viruses such as infectious pancreatic necrosis virus (guppy reovirus) and infectious hematopoietic necrosis virus may apart of the vaccine of the invention (column 6).

As stated above, it is the Examiner's position that the combination of references (Fang et al and Yang et al) renders the claimed invention obvious.

In view of all of the above this rejection is maintained.

10. The rejection under 35 U.S.C. 103(a) is maintained for claim 22 for the reasons set forth on page 18-19 paragraph 13 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim 22 is rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145)* in view of Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* as applied to claims 1-3, 5-6, and 10 and further in view of Morinigo et al *(Bulletin of the European Association of Fish Pathologists, Nov.2, 2002, Vol. 22, No.5, p. 298-303).*

Claim 22 is drawn to the oral vaccine according to claim 1 further comprising bacterial antigens of killed bacteria selected from the group consisting of bacterial antigens or killed bacteria selected from the group consisting of *Shewanella putrefaciens, Pseudomonas florescens, Vibrio alginolyticus* and *Flexibacter columnaris.*

The teachings of Fang et al and Yang et al have been described previously (paragraph 5 above).

Fang et al and Yang et al do not teach vaccines comprising bacterial antigens or killed bacteria selected from the group consisting of *Shewanella putrefaciens, Pseudomonas florescens, Vibrio alginolyticus* and *Flexibacter columnaris.*

Morinigo et al teach that a divalent vaccine composition comprising *Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida.* Morinigo et al teach that the concentration of protein 800 mg ml^{-1} (page 299).Morinigo et al teach that high protection was conferred by the divalent vaccine (page (302).

It would be *prima facie* obvious at the time the invention was made to add the *Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida* antigens as taught by Morinigo et al to the vaccine composition of Fang et al and Yang et al as combined above because Yang et al teach oral vaccines that comprise multiple antigens produce immune response from the same or different pathogens (column 2). It would be expected barring evidence to the contrary that a vaccine comprising proteins from *Aeromonas hydrophila* and *Vibrio alginolyticus* and *Photobacterium damselae subsp.*

Piscicida antigens would be effective in protecting against a broad spectrum of fish diseases.

Applicant's Arguments

Applicant urges that the disclosure of Morinigo et al is relied on for the disclosure of *alginolyticus* and *Photobacterium damselae subsp. Piscicida* antigens. However, Morinigo et al not overcome the deficiencies of Fang et al and Yang et al as described above.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

Morinigo et al teach that a divalent vaccine composition comprising *Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida*. Morinigo et al teach that the concentration of protein 800 mg ml^{-1} (page 299). Morinigo et al teach that high protection was conferred by the divalent vaccine (page (302).

As stated above, it is the Examiner's position that the combination of references (Fang et al and Yang et al) renders the claimed invention obvious.

In view of all of the above this rejection is maintained.

11. The rejection under 35 U.S.C. 103(a) is maintained for claim 45 for the reasons set forth on page 19-20 paragraph 14 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim 45 is rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145)*, Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* and Wang et al *(Fish Shellfish Immunol., Nov. 2002;13(5):337-50)*(Abstract only) as applied to claims 1-3, 5-6, 10-12, 15-16, 20, 27-

32, 35-36 and 48 above and in further view of Wolf-Watz et al (*U.S. Patent No. 5,284,653 published February 8, 1994).*

Claims 45 is drawn to the oral vaccine of claim 11 further comprising an inactivated virus selected from the group consisting of guppy reovirus and guppy nervous necrosis virus.

The teachings of Fang et al, Yang et al and Wang et al have been described previously (paragraph 8 above).

Fang et al, Yang et al and Wang et al as combined above do not teach guppy reovirus and guppy nervous necrosis virus.

Wolf-Watz et al teach a fish vaccine comprising live avirulent invasive bacteria (see the Title and the Abstract). Wolf-Watz et al teach that viruses such as infectious pancreatic necrosis virus (guppy reovirus) and infectious hematopoietic necrosis virus may apart of the vaccine of the invention (column 6). Wolf-Watz et al teach that the bacteria of the invention contains $1x10^2$-$1x10^8$ bacteria/ml (column 8). Wolf-Watz et al teach that the vaccine of the invention can be added to fish feed (column 8).Wolf-Watz et al teach that the invention contemplates vaccines comprising bacteria the carry multiple determinants from different pathogenic fish and capable of expressing hybrid (fusion) determinants (column 7).

It would be *prima facie* obvious at the time the invention was made to add the guppy reovirus as taught by Wolf-Watz et al to the vaccine composition of Fang et al, Yang et al and Wang et al as combined above because Yang et al teach oral vaccines that comprise multiple antigens produce immune response from the same or different pathogens (column 2) and Wolf-Watz et al teach that the vaccine of the invention may comprise one or more antigens that are pathogenic to fish to produce a vaccine that provides broad spectrum protection against a range of fish pathogens (column 7). It would be expected barring evidence to the contrary that a vaccine comprising proteins from multiple antigens would be effective in protecting against a broad spectrum of fish diseases.

Applicant's Arguments

Applicant urges that the combination of prior art references does not teach or suggest the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

As stated above, it is the Examiner's position that the combination of references (Fang et al, Yang et al, Wang et al and Wolf-Watz et al) renders the claimed invention.

12. The rejection under 35 U.S.C. 103(a) is maintained for claim 46 for the reasons set forth on pages 20-21 paragraph 15 of the previous Office Action.

The following rejection is maintained and reiterated below:

Claim 46 is rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145)*, Yang et al *(U.S. Patent No. 6,872, 386 published March 29, 2005)* and Wang et al *(Fish Shellfish Immunol., Nov. 2002;13(5):337-50)* as applied to claims 1-3, 5-6, 10-12, 15-16, 20, 27-32, 35-36 and 48 above and in further view of Morinigo et al *(Bulletin of the European Association of Fish Pathologists, Nov.2, 2002, Vol. 22, No.5, p. 298-303).*

Claims 46 is drawn to the oral vaccine of claim 11 further comprising bacterial antigens of killed bacteria selected from the group consisting of bacterial antigens or killed bacteria selected from the group consisting of *Shewanella putrefaciens, Pseudomonas florescens, Vibrio alginolyticus* and *Flexibacter columnaris.*

The teachings of Fang et al, Yang et al and Wang et al have been described previously (paragraph 8 above).

Fang et al, Yang et al and Wang et al do not teach bacterial antigens or killed bacteria selected from the group consisting of *Shewanella putrefaciens, Pseudomonas florescens, Vibrio alginolyticus* and *Flexibacter columnaris.*

Morinigo et al teach that a divalent vaccine composition comprising *Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida.* Morinigo et al teach that the concentration of protein 800 mg ml^{-1} (page 299).Morinigo et al teach that high protection was conferred by the divalent vaccine (page (302).

It would be *prima facie* obvious at the time the invention was made to add the *Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida* antigens as taught by Morinigo et al to the vaccine composition of Fang et al, Yang et al and Wang et al as combined above because Yang et al teach oral vaccines that comprise multiple antigens produce immune response from the same or different pathogens (column 2). It would be expected barring evidence to the contrary that a vaccine comprising proteins from *Aeromonas hydrophila* , the immobilization antigen repeat I of *Ichthyophythirius, Vibrio alginolyticus* and *Photobacterium damselae subsp. Piscicida* antigens would be effective in protecting against a broad spectrum of fish diseases.

Applicant's Arguments

Applicant urges that the combination of prior art references does not teach or suggest the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 25, 2008 have been fully considered but they are not persuasive.

As stated above, it is the Examiner's position that the combination of references (Fang et al, Yang et al, Wang et al and Morinigo et al) renders the claimed invention.

New Ground of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claim 48 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 48 recites the claim limitation "...the at least one of water and saline...". It is unclear what Applicant intends by this recitation. Does Applicant intend that the antigens are formulated in water or saline? Correction is required.

Status of Claims

14. No claims allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
April 8, 2008

/N. M. Minnifield/
Primary Examiner, Art Unit 1645